ORIGINAL ARTICLE

CORRELATION BETWEEN ANAEMIA AND THROMBOCYTOPENIA IN YOUNGER PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background: Thrombocytopenia needs careful attention of the physician for immediate management to avoid complications. Limited local data is available on low platelet count among patients of all age group on diagnosis of acute lymphoblastic leukaemia (ALL). The aim of this study was to assess the frequency and correlation of anaemia and liver function tests with thrombocytopenia among patients diagnosed with ALL. **Methods:** A prospective study was conducted on patients diagnosed with ALL at Hayatabad Medical Complex, Peshawar. Age, gender, presence of anaemia and deranged liver function tests were correlated with low platelet count in patients with ALL. **Results** A total of 90 patients diagnosed with ALL at the department during the study period were included in the study. Mean age of the patients was 15.43±4.756 years. Among these, 64 (71.1%) were male and 26 (28.9%) patients were female. Low platelet count was observed in 41 (45.5%) of the patients while 49 (54.5%) had platelet count within the range. Low haemoglobin levels were strongly related to presence of low platelet count in our target population (p<0.001). Deranged liver functions were not significantly correlated to thrombocytopenia in patients with ALL. **Conclusion:** Low platelet count was a common finding at the time of diagnosis among patients diagnosed with acute lymphoblastic leukaemia. Presence of anaemia was statistically significantly correlated with presence of low platelet count among the patients at the time of diagnosis of ALL.

Keywords: Acute lymphoblastic leukaemia, ALL, Diagnosis, Platelet, Haematology, Blood, Anaemia

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INTRODUCTION

Haematological malignancies have been diagnosed at much high frequency in last two decades as compared to remote past because of advancements in diagnostic procedures.[1] These malignancies are basically a diverse group of disorders with wide range of symptoms, management plans and prognostic factors.[2] Almost all age groups have been affected by leukaemias or lymphomas, but younger age group has been mostly affected by acute lymphoblastic leukaemia (ALL) as compared to older age group.[3]

Normal haematological parameters are necessary for the overall homeostasis. Platelets are one of the most important components of blood and play the main role in haemostasis on exposure to trauma and other conditions of injury.[4] A lot of haematological malignancies may involve this cell line directly or indirectly.[5] Malignancies which indirectly involve platelets warrant more careful eye of the treating physician to diagnose the abnormality in time for better management and to avoid further complications.[6]

Studies have been performed globally regarding low platelet count in ALL either at time of diagnosis or with response to standard treatment offered for this condition. As per 10 years of study performed by Jaime-Pérez *et al*[7], anaemia and thrombocytopenia at time of diagnosis of ALL were found in 83% of the cases, leukocytosis in 36.6% and leucopoenia in 36.1% of cases. Grunnan *et al*[8] found same phenomenon in patients of ALL after induction therapy and revealed that platelet counts after induction treatment may improve treatment stratification for patients with childhood ALL. Bayhan *et al*[9] reported the incidence of thrombocytopenia purpura, though rare, but the phenomenon cannot be completely ruled out among patients suffering from ALL. Liver functions are not usually affected in initial phases of ALL disease, however, due to systemic spread, diffuse infiltration of tumour cells may result in hepatomegaly in addition to splenomegaly. Recently, different childhood ALL cases with hepatic dysfunction have been reported which may be related to comorbid viral infections, autoimmune hepatitis and obstruction of hepatic arteries by leukemic cells resulting in hypoxia.[10,11]

Haematological malignancies have been commonly encountered malignancies in our part of the world and pose a great burden on our health care budget. Leukaemias if complicated with other problems may lead to increased mortality and morbidity and make things complex both for the patient and the treating team. Limited local data is available low platelet count among patients of all age group at diagnosis of ALL. Sultan *et al*[12] reported that low platelet count was a common finding among adult patients in Pakistan. The present study was planned with the rationale to find the frequency and factors related to low platelet counts especially anaemia and hepatic dysfunction among patients diagnosed with ALL at Oncology Department, Hayatabad Medical Complex, Peshawar.

PATIENTS AND METHODS

This cross-sectional study was conducted at the Oncology Department, Hayatabad Medical Complex, Peshawar, from August 2018 to July 2019. All patients of ALL diagnosed by consultant oncologist/ haematologist on the basis of National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines[13] were included in this study using non-probability consecutive sampling technique. Sample size was calculated by WHO sample size calculator using population prevalence proportion of cytopenia in ALL as 6%.[14] Inclusion criteria included paediatric and young patients between the age of 1 and 25 years diagnosed with ALL waiting for induction therapy. The patients already put on treatment, and those suffering from other conditions such as autoimmune disorders, chronic liver disease, pregnant women, and undiagnosed thrombocytopenia were excluded from the study.

The ethical approval from the Ethical Review Board, and written informed consent from the patients or their caregivers were included in the study. The diagnosis of thrombocytopenia was made with platelet count of less than 150,000/µl[15], estimated through Chemistry Analyser Machine®. Anaemia was described as haemoglobin values of <11 g/dl.[16] Abnormal liver function included either of liver enzymes or bilirubin levels more than normal range.[17] Correlation of age, gender, presence of anaemia and deranged liver function tests was evaluated with low platelet count.

Characteristics of patients and the distribution of the platelet count were described by using the descriptive statistics. Chi-square test was used to determine difference between group variances. Binary logistic regression analysis was done to evaluate the relationship of age, gender, presence of anaemia and deranged liver function tests, and were correlated with low platelet count. All statistical analysis was performed using SPSS-24, and $p \leq 0.05$ was considered significant.

RESULTS

A total of 90 patients diagnosed as acute lymphoblastic leukaemia at our department during the study period were included in analysis. Mean age of the patients was 15.43±4.756 years; 64 (71.1%) were male, and 26 (28.9%) were female. Low platelet count was observed in 41 (45.5%) of the patients while 49 (54.5%) had platelet count within the range. Pearson chi-square analysis (Table-1) showed that low haemoglobin levels were strongly related to presence of low platelet count in our target population ($p<0.001$). Binary logistic regression analysis confirmed this association and patients with low levels of haemoglobin had clearly more chances of having low platelet count as well ($p<0.001$) (Table-2). Odds Ratio with 95% CI was 6.227 (2.402–16.142). Deranged liver functions were not found to be significantly associated with thrombocytopenia in patients with ALL ($p>0.05$).

Table-1: Characteristics of the study group and platelet count in the ALL patients [n (%)]

Patient Demographics		Normal Platelet count	Low Platelet count	*p*
Age	≤12 year	24 (48.9)	14 (34.1)	0.154
	>12 year	25 (51.1)	27 (65.9)	
Gender	Male	37 (75.5)	27 (65.8)	0.315
	Female	12 (24.5)	14 (34.2)	
Deranged liver function	No	24 (48.9)	17 (41.5)	0.475
	Yes	25 (51.1)	24 (58.5)	
Presence of anaemia	No	38 (77.5)	15 (36.6)	<0.001
	Yes	11 (22.5)	26 (63.4)	

Table-2: The correlated factors relating with low platelet count: the binary logistic regression

Demographics	*p*	Odds Ratio (95% CI)
Age (ref. is <12 years)	0.315	1.659(0.619–4.447)
Gender (ref. is male)	0.515	0.698(0.237–2.058)
Deranged Liver functions (ref. is normal liver functions)	0.266	1.722 (0.661–4.486)
Presence of anaemia (ref. is no anaemia)	0.000	6.227 (2.402–16.142)

DISCUSSION

Cancers are one of the leading causes of mortality and morbidity among all age groups all around the world.[1] Variety of laboratory and clinical findings may be part of spectrum of acute lymphoblastic leukaemia. Jawaid *et al*[18] investigated haematological causes of thrombocytopenia in children at Aga Khan University Hospital, Karachi, and concluded that haematological malignancies were one of the commonest causes of low platelet count in the age group. Our study supports their findings as around 40% of patients diagnosed with ALL in our study had low platelet count but no significant correlation was found between low platelet count and paediatric patients with ALL. Abnormal liver function tests were not found to be correlated with thrombocytopenia in patients with ALL.

Adly *et al*[19] published a study in 2015 regarding evaluation of immature platelet count in distinguishing thrombocytopenia in paediatric ALL from immune thrombocytopenia. They found that children diagnosed with acute lymphocytic leukaemia (ALL) had considerably elevated immature platelet fraction (median 10%, $p<0.01$), suggesting that thrombopoiesis is stimulated despite virtual absence of bone marrow progenitors. We did not study immature platelet count or included patients of ITP but found that low platelet count was a consistent finding among patients of ALL. Another study by Bhushan *et al*[20] found the same phenomenon. Considering the high prevalence of thrombocytopenia in patients with haematological malignancies, they tried to establish the presentation of acute leukaemia with normal platelet count at diagnosis. They found that patient with ALL may have normal platelet count with anaemia and

leukopenia. Our findings support their results in general as 65.8% of our male patients had low platelets. Presence of anaemia was a strong predictor of low platelet count in our target population.

Kakaje *et al*[21] from Syria concluded that most patients diagnosed with ALL had either abnormal platelet count (89.3%) or low haemoglobin level (88.8%) when presenting, and only (2.0%) having normal levels for both. They suggested that having normal haemoglobin and platelet count can be used for quick screening in crisis time like in Syria for prioritizing the patients.[21] Both parameters they found deranged in their study participants were also found abnormal in our study subjects, i.e., 26 (63.4%) patients of ALL with low platelet count presented anaemia ($p<0.05$). This shows that anaemia and low platelet count should not be missed before starting the treatment of ALL.

The major limitation of our study was the lack of generalizability as patients from single centre were included in the study with smaller sample size. Patients were not evaluated before the diagnosis of ALL to look for baseline platelet count. Future studies with better design may generate better and generalizable results.

CONCLUSION

Low platelet count was a common finding at the time of diagnosis among patients with ALL but was not significantly correlated to ALL. Presence of anaemia was statistically significantly correlated with presence of low platelet count among these patients at the time of diagnosis of ALL. A large prospective study is recommended for comprehensive correlation between thrombocytopenia and ALL.

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